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Attorney Docket No. 13716  
2058-181

### REMARKS

Initially, Applicants thank the Examiner for noting on the record that Applicants' elected species is 1,2,4-carbonyl di-triazole and for the reference to the nomenclature of the elected species, as commonly known in the art. (Office Action dated March 26, 2003, Par. 9).

The Applicants note that the elected species 1,2,4-carbonyl di-triazole, as the compound is referred to throughout the specification, was inadvertently referred to as 1,2,3-carbonyl di-triazole in numbered paragraph III(D) of Applicants Response dated December 23, 2002.

#### I. Status Of The Claims.

Claims 1-19 are pending in the application. Claims 1 and 5 are rejected under 35 U.S.C. § 112, paragraph 1. Claims 1-4, 9-15 and 18 are rejected under 35 U.S.C. § 102(b), and Claims 1-15 are rejected under 35 U.S.C. § 103(a). Claims 16-17, and 19 are withdrawn. This Response and Amendment amends Claims 1-15, and 18; cancels Claims 16-17, and 19; and adds new Claims 20-25. New Claims 20-25 read on the elected invention and species. The claim amendments are made in the revised format as authorized in the USPTO Pre-OG Notice dated January 31, 2003. The claim amendments and new claims do not add new matter as detailed below. Entry of these amendments is respectfully requested.

#### II. Claim Amendments And New Claims.

##### Claim 1:

Minor format amendments have been made to Claim 1, and the phrase "the biological molecule selected from the group consisting of oligonucleotides, nucleic acids, polypeptides, and carbohydrates" has been added. The listed biological molecules are disclosed on page 4, lines 23-24 of the specification. Accordingly, the amendment to Claim 1 does not add new matter.

##### Claims 2-4:

Minor format amendments have been made to Claims 2-4 for clarity. These amendments do not alter the scope of Claims 2-4 and do not add new matter.

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Minor format amendments have been made to Claim 5, and the phrase "a circular spot at one or more sites on the activated support" has been added for antecedent basis. These amendments do not alter the scope of Claim 5. Depositing a circular spot is further described on page 9, lines 3-5 of the Specification. Accordingly, the amendments to Claim 5 do not add new matter.

**Claim 6:**

Minor format amendments have been made to Claim 6, and the phrase where "one or both of the activating compound and the biological molecule is printed onto the solid support" has been added. Claim 6 is broadened to include printing of the "activating compound" within the scope of the claim. Printing solutions onto the solid support is described on page 9, lines 11-17 of the Specification. Accordingly, the amendments to Claim 6 do not add new matter.

**Claims 7-8:**

Minor format amendments have been made to Claims 7-8, and Claims 7-8 have been amended to reflect the amendments made to Claim 1, upon which Claims 7-8 depend. These amendments do not change the scope of the Claims. Providing and reacting a biological molecule in a humid chamber is further described on page 8, line 21 through page 9, line 10 of the Specification. Accordingly, the amendments to Claims 7-8 do not add new matter.

**Claims 9-11:**

Minor format amendments have been made to Claims 9-11 for clarity. These amendments do not alter the scope of Claims 9-11 and do not add new matter.

**Claim 12:**

A minor format amendment has been made to Claim 1, and a step of "providing a solid support having at least one available amino group, the solid support selected from the group consisting of a bead, a plate, and a film" has been added. Also, the word "identical" has been deleted in reference to the leaving groups  $L_1$  and  $L_2$ . The named solid supports are described on page 6, lines 18-19 of the Specification. Leaving groups (*i.e.*, independently selected leaving groups, that can be the same or different) are described on page 6, line 29 through page 7, line 1 of the specification. Accordingly, the amendments to Claim 12 do not add new

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matter.

**Claims 13-15:**

Minor format amendments have been made to Claims 9-11 for clarity. These amendments do not alter the scope of Claims 9-11 and do not add new matter.

**Claim 18:**

Minor format amendments have been made to Claim 18, and Claim 18 has been amended to reflect the amendments made to Claim 1, upon which Claim 18 depends. These amendments do not change the scope of Claim 18. Accordingly, the amendments to Claim 18 do not add new matter.

**Claim 20 (New):**

Support for new Claim 20 is found in original Claim 1; biological molecules selected from the group consisting of oligonucleotides, nucleic acids, polypeptides, and carbohydrates are disclosed on page 4, lines 23-24 of the specification; and a solid support selected from the group consisting of a bead, a plate, and a film is described on page 6, lines 18-19 of the Specification. Accordingly, new Claim 20 does not add new matter.

**Claim 21 (New):**

Support for new Claim 21 is original Claim 18. Page 11, lines 8-9 of the Specification further describes washing the solid support and unreacted groups. Accordingly, new Claim 21 does not add new matter.

**Claim 22 (New):**

Support for new Claim 22 is original Claim 5. Depositing a circular spot is further described on page 9, lines 3-5 of the Specification. Accordingly, new Claim 22 does not add new matter.

**Claim 23 (New):**

Support for new Claim 23 is original Claim 6. Printing solutions onto the solid support is further described on page 9, lines 11-17 of the Specification. Accordingly, new Claim 23 does not add new matter.

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2058-181**Claim 24 (New):**

Support for new Claim 24 is original Claim 6. Providing and reacting a biological molecule in a humid chamber is further described on page 8, line 21 through page 9, line 10 of the Specification. Accordingly, new Claim 24 does not add new matter.

**Claim 25 (New):**

Support for new Claim 25 is found on page 5, line 19 through page 6, line 1, which describes oligonucleotides having at least one free amino or thiol group. Accordingly, new Claim 25 does not add new matter.

**III. The 35 U.S.C. § 112, Par. 2 Rejection**

Claims 1 and 5 have been rejected under 35 U.S.C. § 112, Par. 2. for the reasons stated in numbered paragraph 11 of the Office Action dated March 26, 2003 (the "Office Action"). In response, Claim 1 has been amended to recite the step of "providing" a biological molecule. Claim 5 has been amended to recite that step (b) "comprises depositing . . . the biological molecule in a circular spot at one or more sites on the activated support". It is believed that this amendment obviates the Examiner's rejection. Withdrawal of the rejection of Claims 1 and 5 under 35 U.S.C. § 112, Par. 2 is respectfully requested.

**IV. The 35 U.S.C. § 102(b) Rejection.**

Claims 1-4, 9-15 and 18 stand rejected under 35 U.S.C. § 102(b) as anticipated by Stolowitz et al (WO 87/06586) for the reasons stated in numbered paragraph 12 of the Office Action. Applicants respectfully request reconsideration of this rejection based on the following comments, insofar as the rejection applies to the amended claims.

Applicants respectfully submit that Stolowitz et al does not describe all of the limitations of the claimed invention. Independent Claims 1 and 20 are limited to a "biological molecule selected from the group consisting of oligonucleotides, nucleic acids, polypeptides, and carbohydrates". The Office asserts that glycine, disclosed in Stolowitz et al. reads on the claimed biological molecule. (Office Action, page 6, lines 7-9). Glycine is not one of an oligonucleotide, nucleic acid, polypeptide, or carbohydrate. Accordingly, withdrawal of the

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rejection under 35 U.S.C. § 112, Par. 2 of Claim 1, and Claims 2-4, 9-11, and 18, depending from Claim 1, and allowance of Claims 1 and new Claim 20 and their dependent claims is respectfully requested.

Applicants respectfully submit that Stolowitz et al. does not describe all of the limitations of the claimed invention. Independent Claims 12 and 20 are limited to a "solid support selected from the group consisting of a bead, a plate, and a film". The Office asserts that Stolowitz et al discloses amine-containing activated supports such as "aminopropyl silica gel". (Office Action page 5, lines 20-23). The Office has not asserted that Stolowitz discloses beads, plates, or films, as claimed by Applicants. Rather, it is Applicants' position that Stolowitz discloses "particulate bonded phase chromatographic supports prepared by silanization of silica gel or controlled pore glass" (Stolowitz, page 3, lines 15-17). Stolowitz further describes the chromatographic supports as "particulate silica or controlled pore glass substrate". The "particulate bonded phase chromatographic supports", as disclosed in Stolowitz, are not a bead, plate, or film, as claimed by Applicants. Accordingly, withdrawal of the rejection under 35 U.S.C. § 112, Par. 2 of Claim 12, and Claims 13-15, depending from Claim 12, and allowance of Claims 12 and new Claim 20, and their dependent claims is respectfully requested.

#### **V. The 35 U.S.C. § 103(a) Rejections.**

Claims 1-6, 9-15, and 18 are rejected under 35 U.S.C. § 103(a) as unpatentable over Stolowitz et al in view of Milton (U.S. 6,146,833) for the reasons stated in numbered paragraph 16 of the Office Action. Claims 1-15, and 18 are rejected under 35 U.S.C. § 103(a) as unpatentable over Stolowitz et al in view of Milton (U.S. 6,146,833), Okamoto et al (U.S. 6,476,215) and Guo et al (Nuc. Acids Res. 1994, pp. 5456-5465) for the reasons stated in numbered paragraph 17 of the Office Action. Applicants respectfully request reconsideration of the § 103(a) rejection based on the following comments, insofar as the rejection applies to the amended claims.

To establish a *prima facie* case of obviousness, the Office must provide a suggestion or motivation, either in the references themselves or in the knowledge generally available to one

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of ordinary skill in the art, to modify the reference, or to combine reference teachings. MPEP § 2143. It is Applicants' position that the Office has not provided this suggestion or motivation and thus has not established a *prima facie* case of obviousness.

As discussed in paragraph IV above, Claims 1 and 20 are limited to attaching a biological molecule, namely "oligonucleotides, nucleic acids, polypeptides, and carbohydrates" to a solid support, and Claims 12 and 20 are limited to attaching a biological molecule to a "solid support selected from the group consisting of a bead, a plate, and a film". Stolowitz does not teach or suggest these limitations.

**A. The 35 U.S.C. § 103(a) rejection over Stolowitz et al in view of Milton.**

The Office points to Milton for **depositing** biological compounds onto solid supports by printing. (Office Action, page 7 lines 17-19). However, Milton does not teach or suggest "attaching" Applicants claimed biological molecules to Applicants claimed solid supports.

It is Applicants position that the Office has not provided a suggestion or motivation to combine Stolowitz's "reacting molecules with amine-containing, activated supports" as stated by the Office, with Milton's biological compounds to arrive at Applicant's invention. To establish *prima facie* obviousness, the Office must show something more than that the invention was obvious to try; it must show that the prior art motivated the skilled artisan to make the claimed invention. Moreover, the requisite teaching or suggestion to modify a reference must be found in the prior art, and cannot be derived from Applicants' own disclosure. See, MPEP § 2143; MPEP § 2141.

There is no motivation to modify Stolowitz, or combine Stolowitz with Milton to arrive at Applicants' claimed invention. Stolowitz teaches that the invention "**eliminates** the adsorption of biological macromolecules and low molecular weight amines observed with bonded phase supports which are not further derivatized." (Stolowitz, page 4, lines 6-9, emphasis added). Thus, the invention described in Stolowitz precisely teaches away from that which Applicants claim, namely attaching biological macromolecules (*e.g.*, oligonucleotides, nucleic acids, polypeptides, and carbohydrates) to a solid support and the Office has not pointed to Milton to remedy this deficiency.

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**B. The 35 U.S.C. § 103(a) rejection over Stolowitz et al in view of Milton, Okamoto et al., and Guo et al.**

The Office admits that Stolowitz lacks the specific teaching of depositing compounds in a particular area on the support and the use of a humid chamber. The Office points to Milton, Guo, and Okamoto for the proposition that printing or spotting techniques to deposit biological compounds onto solid supports was established at the time of filing. (Office Action, page 8 lines 17-21). The Office further points to Guo and Okamoto for the use of a humid chamber. However, Milton, Guo, and Okamoto do not teach or suggest "attaching" the biological molecule (*i.e.*, oligonucleotides, nucleic acids, polypeptides, and carbohydrates as specified in Claims 1 and 20) to the solid support (*i.e.*, a bead, a plate or a film as specified in Claims 12 and 20). As noted in Paragraph V(A) above, the invention described in Stolowitz does not teach Applicants claimed solid supports, and precisely teaches away from attaching biological macromolecules (*e.g.*, oligonucleotides, nucleic acids, polypeptides, and carbohydrates) to a solid support. The teachings in Milton, Guo, and Okamoto of depositing by printing or spotting, or the use of a humid chamber, as asserted by the Office, do not suggest the desirability of the combination.

Based on the forgoing comments, withdrawal of the rejection of under 35 U.S.C. § 103(a) and allowance of all Claims is respectfully requested.

### CONCLUSION

The Applicant believes that all pending claims, Claims 1-15, 18, and 20-25, are in condition for allowance and such action is earnestly requested. If the present amendments and remarks do not place the Application in condition for allowance, the Examiner is encouraged to contact the undersigned directly if there are any issues that can be resolved by telephone with the Applicants' representative.

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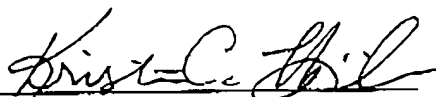
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The Commissioner is authorized to charge \$36, for the two excess Claims over 20. No other fees are believed due by this Response. If, however, any other fees are due, the Commissioner is authorized to charge any other fees associated with this Response and Amendment to Deposit Account No. 19-2090.

Respectfully Submitted,  
SHELDON & MAK PC

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By



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